INTERNATIONAL SEARCH REPORT

PCT/GB2004/004401

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N5/00 C12N5/06 C07K14/475

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HOLLNAGEL ANGELA ET AL: "Id genes are direct targets of bone morphogenetic protein induction in embryonic stem cells" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 28, 9 July 1999 (1999-07-09), pages 19838-19845, XP002324467 ISSN: 0021-9258 abstract -/--	1

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2005	29. 08. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Nichogiannopoulou, A

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Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	YING QI-LONG ET AL: "BMP induction of Id proteins suppresses differentiation and sustains embryonic stem cell self-renewal in collaboration with STAT3." CELL, vol. 115, no. 3, 31 October 2003 (2003-10-31), pages 281-292, XP002288135 ISSN: 0092-8674 the whole document	1-21,23, 41-43, 49-51
P,X	TEMPLE SALLY: "Embryonic stem cell self-renewal, analyzed." CELL, vol. 115, no. 3, 31 October 2003 (2003-10-31), pages 247-248, XP002324469 ISSN: 0092-8674 the whole document	1-21,23, 41-43, 49-51
X	REUBINOFF BENJAMIN E ET AL: "Embryonic stem cell lines from human blastocysts: Somatic differentiation in vitro" NATURE BIOTECHNOLOGY, NATURE PUB. CO, NEW YORK, NY, US, vol. 18, no. 4, April 2000 (2000-04), pages 399-404, XP002195338 ISSN: 1087-0156 page 403, right-hand column, paragraph 1	3-9,11, 12, 15-18, 21,41, 42,49-51
P,A	DAHERON LAURENCE ET AL: "LIF/STAT3 signaling fails to maintain self-renewal of human embryonic stem cells" STEM CELLS (MIAMISBURG), vol. 22, no. 5, 2004, pages 770-778, XP009046296 ISSN: 1066-5099 abstract	1
A	FINLEY M F A ET AL: "BMP-4 INHIBITS NEURAL DIFFERENTIATION OF MURINE EMBRYONIC STEM CELLS" JOURNAL OF NEUROBIOLOGY, JOHN WILEY AND SONS., NEW YORK, NY, US, vol. 40, no. 3, 5 September 1999 (1999-09-05), pages 271-287, XP009017895 ISSN: 0022-3034 the whole document	1

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 41-43 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-21, 23, 41-43, 49-51

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[X] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 41-43 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Present claims 3-30, 34, 41-43 and 49-51 relate to agents defined by reference to a desirable characteristic or property, namely their ability to increase Id protein expression or activity.
The claims cover all agents having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT only for BMP, serum, fibronectin and Nanog (see p. 32 and 36). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the agents by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.
Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the effect of BMP, fibronectin, serum and Nanog on stem cells.

Present claims 7 and 30 relate to agonists, activators and homologues defined by reference to a desirable characteristic or property, namely their ability to induce Id protein expression or activity.
The claims cover all agents having this characteristic or property, whereas the application provides neither support within the meaning of Article 6 PCT nor disclosure within the meaning of Article 5 PCT for any such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the agents by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

The present set of claims refers to the promotion of self renewal of any and all pluriopotent cells in culture. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT however, is only given for mouse ES cells (see Examples). It is well known in the art that pluriopotent cells from different species and different cell types from the same species respond differently to signaling molecules. Therefore claims based on extrapolation from mouse ES cells to mammalian pluripotent cells in general are not supported and subject-matter thereof not disclosed under Art.5 and 6 PCT,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

respectively. Consequently a search has been carried out for those parts of the claims refering to mouse ES cells.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 2, 13, 14 completely and 4-6, 8-12, 15, 16, 18, 49-51 partially

   Use of an Id gene product in promoting self-renewal of pluripotent cells in culture.

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2. claims: 3, 7, 17, 19-21, 23, 41-43 completely and 4-6, 8-12, 15, 16, 18, 49-51 partially

   Use of an agent that increases Id protein expression or activity in promoting self-renewal of pluripotent cells in culture.

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3. claims: 22, 45-48

   Methods for directing differentiation of ES cells

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4. claims: 24-30

   Methods for deriving pluripotent cells from blastocysts.

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5. claims: 31-33

   Vectors comprising an Id gene.

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6. claims: 34-40

   Compositions comprising an Id protein

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7. claim: 44

   Cells obtained by the methods of inventions I or II.

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8. claims: 52-55

   Assays for Id protein substitutes
